

Dear Bruce:

Your letter of the 17th received yesterday, the ms. a few days before, but today was the first chance I had to get to it. When I finally did, I enjoyed it thoroughly-- hope my amendment does not seem too abandoned. The details are marked as far as I can on the ms. Some general points:

Terminology: especially transduction. Treated in situ.

Punctuation: I admire your persistence, but I think there are too many semicolons. In general your own criticism is well taken. The experimental parts are quite brisk, the introduction rather overworded. Fat has its uses, but I've suggested some places where it can be trimmed. As you say, I think have have brought in a number of side-issues which not only take up space but may distract the reader from the main argument. This is as clear as could be, however.

Do you wish to discuss authorship any further? I gather that after you decided not to assume it to yourself, as I originally suggested, that I might still exercise my own option. I would still prefer the first plan, but recognize Norton's vested interest in vetoing it, and will in fact agree (after more prolonged judgment) that the triple authorship is wiser. The advantages, of expedition and simplicity, are already abandoned, so there is no point in reviving my first proposal.

I am sorry, in a way, to report that SW-553 also shows a linked transduction. (2/60 LT-2 --x SW-967 (another isolate of 553) were 1:--.) It was originally detected on g.. serum agar, later with isolated swarms on straight semi-solid. Is it worth the trouble to bring that in here? I have no personal ~~objection~~ predilection, one way or the other, but suspect you might rebel at the idea of including anything new. There may be some circumstantial evidence of a partial homology of SW-967 with SW-666. They transmotilize each other all right, but the ratio of tracks to swarms seems rather higher than when, e.g., SW-666 Fla⁺ --x SW-967. SW-666 --x 967 is the one that shows such tremendous tracks (best followed over a period of two to three days (sic) in tubes of semisolid inoculated at the surface. I would estimate the full length of some of these tracks at over 30 mm (over 2 cm in projection), and several hundred microcolonies. No major branchings. LT2--x541 and --x 548 were reported as 1:1,2... I have about half ml. of absorbed 2 serum; 2 is a difficult reagent and no longer recognized in the scheme.

Felix may be playing games. I've been corresponding with him on the same points; Boulgakov phage, and stability of O-901. I compared his own old isolates with our stocks, they look pretty much alike.

Am sending SW-970, 972. The latter was labelled as "aberrant gallinarum" by Kauffmann. They are ~~both~~ completely stable, with or without any FA tried, but 970--x SW666 and 972--x666 have both given b:- and g..:-. They transduce motility to some Fla- but not others (3,5,8 and 4,5,8) and so may be tangible examples of stability by multiple Fla-. The homology tests seem your business more than mine: want to try them?

See what K says about SL-13! Edwards takes a dim view of this kind of analysis for the instant purpose: the differences may be essentially quantitative. Fullorum strains labelled XII₁ XII₂ and XII₁ XII₂ seem equally susceptible to PLT22. But he did give me some durazzo and XII₂ strains and serums which should give the necessary reagents if I can get around to the cross-absorptions.

antigenic

I am not so sure of differences between early and late swarms, but there are definitely some much earlier than others (the later taking 18-24 hours)

Phage on solid.

Arthur

✓

I don't recommend saying anything at all about K-12 recombination, if it can be helped. The differences have been gone into in the previous papers where they are more relevant. The best way to avoid any confusion is not to mention K-12 at all.

I am hoping that Nort' may pay us a visit in connection with Federation Meetings in Chicago second week of next month. It will be a chance to coordinate some of our misdirections, if you can return comment by then (if necessary).

Good luck on your possible appointment. It isn't, by any favorable chance, this side of the Atlantic, is it?

Do you know a chap named Aleck Bernstein? He has an M.D. and a Dipl. Bact. from your place, would like to work for a Ph.D. here. I think I'll probably take him, but would welcome any comment or advice. (My judgment of English bacteriologists may be colored by recent wonderful experiences).

[Lab, next day] The paragraphs that follow have been written at odd intervals, and may be disconnected.

I can confirm tracks and occasional swarms from pullorum—x O-901 and gallinarum—x O-901. In view of the apparently rather low efficiency of transduction in this system it may or may not be easy to make an adequate test of H_1 transduction. I hope you don't mind that I duplicate your attempts: as you will note from my last letter I have been engaged with this, but with rather negative results so far. I am especially surprised at having been unable to transduce Mal+ from gallinarum to pullorum, but have now to try a Mal+ pullorum as donor.

I suggest that a more explicit treatment be given of the behavior of O-901. This is probably the most widely familiar O strain, and some readers are bound to try some experiments with it. I have not tried a complete homology test, but it might be sufficient to ~~emphasize~~ emphasize that ~~the~~ O-901 (including authentic strains from Felix) have not only reverted spontaneously, but have given additional additional tracks and swarms, all d, x—LT-2. In fact, it might be a good idea to use this as a way to emphasize the efficiency of the selective technique, quoting Felix (J Hyg 49:94) to show its stability for 28 years in ordinary culture) and also to minimize any sense in which the discrepancy might be regarded as reflecting on F.

When we first discussed this, I had not seen your paper and did not realize how much genetics you would be able to communicate. I leave to your judgment (as of course all the rest of these remarks; ~~they~~ the only thing I have any strong brief for is the rectification of transduction-transformation) whether to add the paragraph at p. 35 justifying the concept of linkage. ~~It~~ I think if you introduce this concept at all, and I admire ~~the~~ your success in clarifying it at this level, that a little more should be said about it. On the other hand, I would not want to preempt a more extensive discussion ^{which} ~~and~~ I hope we can elaborate at some future date when the 666-SL-13-SW553 relationships are further clarified.

Edwards' report just in on the motilized forms of the following, being sent along with SW-970, 972. Here is a fuller listing:

SW	Edwards	motilized: reported serotype	remarks
963	4936-50	i:1,2) relationship??
964	4937-50	i:1,2	
965	no good record	i:-- monophasic	

"Zelly"-1950-Seattle

These had been recorded simply as group B. They were motilized with x— LT-2; I will check using x— other serotype to be sure.

970	3821-52	D nonmotile	g..	not motilized but --x SW666
971	5465-52	D nonmotile(Texas)	gm:-(enteritidis)	
972	1553-52 (= Kauffmann's 151-52)	g...		not motilized but --x SW666

I will see whatever further information I can get, but the records are often fragmentary, and it is considerable trouble to Edwards to trace them back. [If they had the money they could use an IBM system!]

May I retain the tables? I can indicate my remarks here as well as on the sheets.

Table 1: a more explicit designation of LT-2 (which is only the phage type) is Lilleengen # 85 (isolated in 1946 from an outbreak at Stoke Mandeville— Lilleengen p.68 JT may know more about this.) I am beginning to find LT-2 somewhat awkward, and would second (but not initiate) a suggestion to ~~rename~~ rename it TMI or something of the sort(TM2?). This would at least already carry the connotation of typhimurium in , e.g., TM2 --X If we don't alter it now, we'll be stuck with it forever; it would still be time at present, and the equivalence could be put in the table. Add O-901 to the table, and let us adopt Felix' oldest transfer as our type. Have you been able to track down, in print, the explicit history of O901? The only paper I haven't looked at yet (library trouble) is Felix 1930, Lancet.

SW534: add Sertic-Boulgakov reference for VIII-133

533: Edwards # 157 (N25 is ~~is~~ a lab. designation.) There is a reference to this, perhaps not essential here, Edwards & Bruner J. Bact 52:494 (though Cherry actually did this). I have not seen the phenomenon again, having always gotten z₃₃ rather than 1,2. It is not absolutely excluded (Cherry is not too clear about it) that the three occurrences were progeny of a single mutation. Other monophasic --1,2 have behaved as Fla₂ alleles. ~~Edwards' 157~~

[I've told you about finding an old stock culture labelled SW533 which was a mixture of the diphasic resembling SW703 in its fermentations and the --12 monophasic resembling #157]

~~157~~

SW541 : I quote ~~Edwards' 157~~ Kauffmann's letter (3/31.52)

" Nr. 13 = S. typhimurium 3173 "	SW544
" Nr. 58 = S. typhi O 901 "	542
" Nr. 223 = S. typhimurium var. copenhagen 1810 "	SW541
" Nr. 248 = S. paratyphi B O 19 "	SW 543

Edwards' 13 has the same description as Kauffmann's. Ditto 58. They must have a common list (up to a point).

4

SW552. Have you been able to do anything with this particular isolate? It has been implacably rough to me. Its history as far as known is on the enclosed photostat. I have not yet had a reply from Davila. All the Salmonellas indicated are gp:-

TABLE 3a. For typography, I suggest 1:1... for diphasic forms. The third column is redundant, and could be implied in heading or footing to the table, This could save considerable space by permitting it to be set up in a single column width. Id. for columns 2-3-4 of 3b.

TABLE 2. Cultures reported as TM by Edwards are 1:1,2... (I must have mentioned this supra.)

What are your frequencies of a,i in TM2 (sic)—x SL13. As I recall, I found 2:2. It might be worth mentioning (if you concur) the very low yields in this transduction.

You've gotten a motile from SW573 in two steps, haven't you?

I would put "Spontaneous" before mutation in heading, column 4. SW534Fla⁺ is also 1,2...

Is table 5 necessary? The data could be given more compactly in text, where they are essentially repeated ~~anywhere~~ anyhow.

Table 4. Is effect of SL18 on 573 consistent? rather ~~like~~ + S and F as symbols, why not define + as fast swarms, and omit F as symbol.

* ———
mendelian Inset, page 25 and innumerable factors controlling chloroplast development in maize, of which 73 were already catalogued twenty years ago (de Haan, H. 1933 Inheritance of chlorophyll deficiencies. Bibliographica Genetica, 10: 357- 416). Ha! You could also quote many factors affecting the tail in mice (Gruneberg). There does not seem to be a more recent cataloguing of plastid effects. This happens to be the most common type of mutant seen in most plants. I just remembered a reference you should quote: Lewin on nonflagellated and paralyzed Chlamydomonas: JGM 6:233 1952, esp. 242. I have been trying to stimulate further his already active awareness of serological possibilities.

Add:

ACKNOWLEDGMENTS

..... The work at Madison has been supported by [fellowship to B.A.D.S. [?] from the Commonwealth Fund and by] grants ~~from the National Institute of Health~~ (E72-C4) from the National Microbiological Institute of the National Institute of Health, U. S. Public Health Service, from the Rockefeller Foundation, and from the ~~Wisconsin Alumni Research Committee~~ Research Committee of the Graduate School from funds supplied by the Wisconsin Alumni Research Foundation. This paper is recorded as No. 516 from the Department of Genetics, Agricultural Experiment Station, University of Wisconsin.

We are indebted to ...Kauffmann, Felix, Edwards, Taylor, Boulgakov, Lilleengen, Leifson for generously providing cultures and other materials.

The genetic analysis of the linked transductions is being ~~studied~~ *carried* further, but two lines of evidence may be quoted in support of this interpretation. ~~The ability to give swarms whose flagellar antigens~~
 The two O strains, SW 543 and SL 13 have been exposed to lysates of numerous other types in addition to *S. typhi-murium*, and in each case where swarms were produced a minority of these conformed to the ~~flag~~ flagellar type of the donor strain. Thus, in addition to the ~~st~~otype IV V XII b:—, SW 543 has engendered other monophasic types/ such as IV V XII a:—, IV V XII c:—, and IV V XII ² ~~st~~:— when exposed to ~~lysates~~ lysates of *S. sendai*, *S. altendorf* and *S. heidelberg*, respectively. Similarly, SL 13 produced, in addition to I II XII a:—, swarms of the type I II XII r:— when exposed to lysates of *S. heidelberg*. As some of these types have never been reported previously, their present existence provides whatever testimony may be needed to exclude the possibility of contamination in these experiments. Some of the monophasic types produced in this way may be expected to provide antigens useful in the preparation of diagnostic H antisera, (cf. Edwards and Bruner '49).

~~Further consideration has been given to the possibility that in the~~
 cited experiments, where SW 543 gave rise to ~~b:— and i:—~~ ^{to two types of} type swarms, ~~after exposure to a lysate of S. typhi-murium, the two types represent~~
~~the transductions of two different single genetic factors, rather than of two~~
 linked factors in the latter case. However, lysates prepared from such i:— ^{derivatives}
 were again able to evoke both B:— and i:— ^{swarms} from SW-543, and the same "backcross"
~~test has been repeated for two additional generations.~~ ^{derived} The ability of the i:—
~~derived from SW 543, again to evoke two transduction types from its parent SW543~~
 is given as evidence that ^{it} ~~the i:—~~ had received two elements from *S. typhimurium*,
 as distinguished above.

Section I

Introduction: The Phenomenon of transduction (Z&L '52, 1, 2, 3, 4, 51)

Hereditary properties can be transferred or transduced from one *Salmonella* strain to another by means of cell-free culture filtrates.

~~To demonstrate transduction~~, a donor *Salmonella* was lysed by a suitable phage (or otherwise treated to the same effect), and the lysate filtered. ~~excluded~~ The filtrates contained an agent which ~~was~~ transferred various cultural characteristics from the donor ~~strain~~ to a small proportion of ~~the~~ exposed recipient cells, of another strain. As a rule, a maximum per million of one recipient cells was altered, even under optimum conditions. Cells which had thus acquired a new characteristic by transduction transmitted ~~this~~ it through an unlimited number of generations, as far as has been tested.

~~Hereditary~~ Hereditary changes, so-called transformations, have been described in the pneumococcus, and in *Haemophilus influenza* under the influence of cell-free lysates of other strains, ~~and~~ As these are now recognized as being also based on the transfer of ~~hereditary~~ genetic factors, transduction may occur commonly among bacteria. In these organisms, however, the active principle depends on the content of polymerized desoxyribonucleic acids in the lysates, and its activity is destroyed by exposure to desoxyribonuclease(). The transducing activity of *Salmonella* lysates is, however, insusceptible to this enzyme, and is apparently associated with phage particles themselves (Z&L 52)

Bruce: I have suggested this recast for two reasons: 1) the distinction between transduction and transformation was improperly drawn(I regard transformation as too vague a term to dignify so important a phenomenon, but these particular instances of "transformation" are indubitably transductions, as defined in Z&L. Many other "transformations" in bacteriology are equally certainly not. 2) I think you may have repeated too much evidentiary detail from Z&L— the reader get this directly, if necessary, and the conclusions are better emphasized